

REMARKS

Applicant's attorney wishes to thank Examiner Kishore for the courtesies extended during the telephone interview of July 14, 2004. During that telephone interview, it was noted that the claims have been limited to liposomes containing lycopene. Moreover, it was noted that the method of preparing the liposomes as claimed makes a significant difference in the stability of the liposomes. It is critical to the present invention that first the liposome-forming lipid be dissolved in an organic solvent (close to saturation), and only then is the lycopene added. Data showing the differences in stability between liposomes prepared according to the herein claimed method *versus* liposomes prepared by conventional methods can be found in the specification in Table 6B, page 28.

Claims 50-55, 58-84, and 88-89 currently appear in this application. The Office Action of March 5, 2004, has been carefully studied. These claims define novel and unobvious subject matter under Sections 102 and 103 of 35 U.S.C., and therefore should be allowed. Applicants respectfully request favorable reconsideration, entry of the present amendment, and formal allowance of the claims.

Rejections under 35 U.S.C. 112

Claims 50-82 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner alleges that it is unclear how one can obtain a suspension and not a solution when the carotenoid, which is lipophilic, is added to a solution of a phospholipid in an organic solvent as recited in claim 50. Claims 68-74 claim "effective amounts", which the Examiner alleges has no meaning if the disease to be treated is not recited in the claims.

This rejection is respectfully traversed. Claim 50 has been amended to recite that addition of the lycopene to the dissolved liposome-forming lipids forms a mixture of lycopene and liposome-forming lipids. It is immaterial for purposes of the present invention whether the lycopene is completely dissolved in the organic solvent or is merely partially suspended and partially dissolved in the organic solvent. The important feature is that the lycopene and liposome-forming lipids are mixed together in the presence of an organic solvent.

Claims 68-74 have been amended to recite "pharmaceutically and cosmetically effective amounts." The term "effective amount" is defined in the present application

at page 3, lines 17-26, as that determined by such considerations as are known to those versed in the art. The amount of carotenoid carried by the liposomes must be sufficient to achieve a desired therapeutic effect, e.g., to treat, prevent or ameliorate symptoms associated with a disease against which the carotenoid is effective, to lessen the severity or cure the disease, or to prevent the disease. Particularly, the effective amount of the carotenoid is such that it acts against the harmful effects of undesired oxidation of lipids, proteins, tissues or cells in the living body, for example, by environmental hazards, which can exert damage.

As disclosed in the specification as filed, page 1, line 22 to page 2, line 3, lycopene and similar compounds exert a protective action against certain types of diseases, including cancer, heart disease, and other diseases which have radical or oxidant involvement. Thus, lycopene can be used pharmaceutically, and claims 68-74 now claim a pharmaceutically effective amount, the specific amount, of course, being readily determined by one skilled in the art without undue experimentation, depending upon which disease is to be inhibited or prevented.

Art Rejections

Claims 61-78 and 80-82 are rejected under 35 U.S.C. 102(b) as being anticipated by Meybeck.

This rejection is respectfully traversed. While Meybeck describes topical formulations containing a retinoid or a structural analogue thereof, such as β -carotene, there is nothing at all in Meybeck relating to encapsulating lycopene in liposomes.

Claims 61-82 are rejected under 35 U.S.C. 102(b) as being anticipated by Smith.

This rejection is respectfully traversed. Smith does not teach encapsulating lycopene. Smith only describes a free radical quenching composition comprising a liposome containing at least two antioxidants selected from β -carotene, vitamin E, vitamin C, glutathione, niacin, and optionally trace metals such as Zn, Se, Cr, Co, Mn.

Claims 61-78 and 80-82 are rejected under 35 U.S.C. 102(b) as being anticipated by Stahl et al.

This rejection is respectfully traversed. Stahl et al. disclose mixtures comprising liposomes and a carotenoid. Although lycopene is mentioned, there is no teaching in Stahl et al. of encapsulating the antioxidant, such as lycopene, in the liposomes. Stahl merely refers to a mixture (incubation together) of liposomes and the antioxidants and the effect the

antioxidants have on the oxidation damage caused by oxidation of the lipids forming the liposomes. In Stahl et al., the antioxidant merely prevents oxidation of the liposomes. This is not at all the same as the present invention, in which the lycopene is the active ingredient incorporated in the liposome.

Claims 61-78 and 80-82 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meybeck. The Examiner concedes that Meybeck is different from the present invention, as Meybeck dissolves the phospholipid and the carotenoid in an organic solvent and removes the solvent to prepare a dry preparation, whereas the instant application first dissolves the lipid in the organic solvent and then carotenoid is added to the solution.

This rejection is respectfully traversed. The amounts of phospholipid used and the order of the steps for preparing the liposomes are critical. In the present invention, it is essential that first the liposome-forming lipid be dissolved in an organic solvent (close to saturation), and only then is the lycopene added. This order of addition is critical in obtaining stable formulations. Table 6B of the instant specification, page 28, shows that formulations prepared according to the method of the present invention, i.e., first dissolving the lipid, and only then

dissolving the lycopene, results in a formulation that is more stable as compared to those prepared by first dissolving the carotenoid, and only then, the lipid (formulations S02 and S04). As stated in lines 8 and 9 of page 28, Formulations S02 and S04 were less stable. Thus, it is respectfully submitted that the method of preparation is critical to the present invention, and there is nothing in Meybeck that would lead one skilled in the art to dissolve the phospholipid prior to adding the lycopene. There is nothing in Meybeck that would lead one skilled in the art to believe that the order of addition made a difference in the stability of the encapsulated lycopene.

Claim 55 is rejected under 35 U.S.C. 103(a).

This rejection is respectfully traversed. Mackaness et al. disclose prepping liposomes using cyclohexane as an organic solvent. However, Mackaness et al. merely disclose liposomes containing X-ray contrast media, not lycopene. As noted above, the order of addition of components to the organic solvent is critical in forming stable liposomes, and there is nothing in either Meybeck et al. or Mackaness et al. that would lead one skilled in the art to prepare liposomes by first dissolving the liposome-forming liposome in an organic solvent and then adding the lycopene.

Appln. No. 10/073,365
Amd. dated June 2, 2004
Reply to Office Action of March 5, 2004

Entry of the present amendment is earnestly solicited, as it places the claims into condition for allowance, and raises no new issues. Claims directed to preparing liposomes loaded with lycopene have previously been considered (claims 56-57 and 86-87).

In view of the above, it is respectfully submitted that the claims are now in condition for allowance, and favorable action thereon is earnestly solicited.

Respectfully submitted,

BROWDY AND NEIMARK, P.L.L.C.
Attorneys for Applicant

By



Anne M. Kornbau

Registration No. 25,884

AMK:jab
Telephone No.: (202) 628-5197
Facsimile No.: (202) 737-3528
G:\BN\C\ohn\Barenholz8a\Pto\draft.amd.doc